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# Penn Vet Research on Niemann-Pick Disease Paves the Way for Human Clinical Trial

BY JILLIAN MARCUSSEN

**N**iemann-Pick type C disease (NPC) is a rare and incurable neurological disorder that affects one in 120,000 people worldwide. Presently, there are no therapies approved by the U.S. Food and Drug Administration to treat NPC.

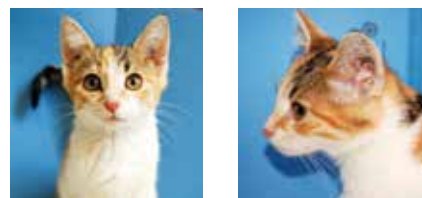
But Dr. Charles Vite, associate professor in neurology and neurosurgery in the Department of Clinical Studies at Penn Vet, is hopeful that this will soon change. In January, a clinical trial began at the National Institutes of Health to test a potential drug called cyclodextrin to treat NPC in children. Research by Dr. Vite paved the way for this Phase I trial, which offers hope for helping both humans and animals who suffer from NPC.

The disease is caused by the accumulation of excessive amounts of cholesterol and glycosphingolipids in the brain and other organs. Affected children are born clinically normal and then experience progressive ataxia, swallowing problems, seizures and impairment of motor and intellectual function in early childhood, and usually die in adolescence.

NPC also occurs naturally in animals. Cats, normal at birth, develop progressive ataxia and impaired motor function, with death occurring by six months of age due to the neurological disease.

The collaborations that led to this clinical trial began in 2006, when Dr. Forbes Porter began a natural history study at the NIH to identify clinical and biochemical disease progression in patients with this rare disease.

At about the same time, researchers at the University of Arizona and the University of California, San Francisco



discovered a disease modifying drug, 2-hydroxypropyl-beta-cyclodextrin (HPBCD). HPBCD is used to increase the solubility and dissolution rate of poorly water-soluble drugs. While the FDA considers it a safe, inactive pharmaceutical ingredient, it is not approved and marketed as an active pharmaceutical.

Further studies performed in the mouse at the Albert Einstein School of Medicine and at the University of Texas Southwestern Medical Center identified HPBCD as effective in treating NPC. Studies in affected cats at Penn Vet identified that administration of the drug intrathecally (into the spinal fluid around the brain) resulted in the most effective therapy of Central Nervous System disease.

“Cats with NPC treated with intrathecal HPBCD are alive and well at over two years of age,” Dr. Vite said. “It works wonderfully.”

Based on the exciting discovery in animals, the Therapeutics for Rare and Neglected Diseases program in NIH’s National Center for Advancing Translational Sciences facilitated collaboration to advance research on cyclodextrin. Dr. Vite teamed with researchers from NIH, Washington University in St. Louis, Janssen Research and Development of Johnson & Johnson, and others to fine tune the therapy.

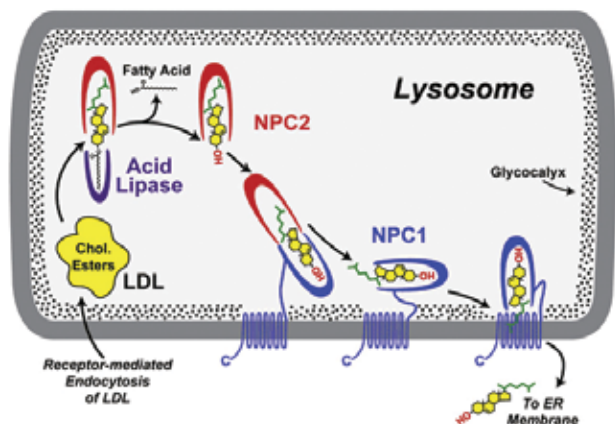
Penn Vet researchers discovered an effective route of drug delivery for NPC, allowing cyclodextrin to reach the nervous system through the spinal fluid. The NIH clinical trial, headed by Dr. Porter, is now using this method to deliver cyclodextrins to children with this disease.

“It doesn’t get any better than finding something that treats animals and then will go on to treat kids,” Dr. Vite said.

The formation of a scientific collaboration involving academic, industry, government, and nonprofit patient advocacy organizations allowed the successful translation of HPBCD from the laboratory setting to a Phase I clinical trial in a rare disease in a relatively short period of time. If safety is demonstrated, the Phase II trial will follow.

“I feel very thankful to be a part of this collaborative effort,” says Dr. Vite.

For a list of research supporters, visit [www.vet.upenn.edu](http://www.vet.upenn.edu).



Mutations in either the *NPC1* or *NPC2* gene result in NPC with *NPC1* mutations accounting for 95% of the cases and responsible for the disease in cats. Kwon et al (2009) Cell 137: 1213-1224